

## Overactive Bladder Medication Adherence When Medication is Free to Patients

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**Purpose:** We examined overactive bladder medication compliance in a health care system in which patients do not pay for medication.

**Materials and Methods:** Pharmacy dispensing records were reviewed for antimuscarinic agents from January 2003 to December 2006 for the United States Military Health System National Capital Region. Medication nonpersistence, switching and adherence were examined. Kaplan-Meier survival analysis was done to compare medication persistence duration.

**Results:** Overactive bladder medications were dispensed to 7,879 adults. Tolterodine extended release (4,716 patients or 60%) and oxybutynin immediate release (2,003 or 25.5%) were most commonly prescribed. The medication nonpersistence rate, defined as the proportion of patients who never refilled a prescription for antimuscarinics during the study period, was 35.1% (2,760 of 7,858). Of 5,098 patients who refilled a prescription 1,305 changed the medication or dose at least once for a medication switch rate of 25.6%. The overall median medication possession ratio, defined as the total days of medication dispensed except for the last refill divided by the number of days between the first dispense date and the last refill date, was 0.82 in all cases. Men had a significantly higher median medication possession ratio than women (0.86 vs 0.81,  $p < 0.001$ ). Of patients who obtained at least 1 refill women remained on medication longer than men (median 606 vs 547 days,  $p = 0.01$ ). Patients on tolterodine extended release had a higher medication nonpersistence rate than those on oxybutynin immediate release (0.89 vs 0.68,  $p < 0.01$ ). There was no difference between extended release medications.

**Conclusions:** In a health care system in which patients do not pay for medications 35% of patients did not refill a prescription for overactive bladder medication, similar to previous reports. However, other measures of medication compliance were higher than those published previously in systems with copays.

**Key Words:** urinary bladder, overactive; muscarinic antagonists; delivery of health care; military personnel; medication adherence

OVERACTIVE bladder is a common condition estimated to affect 16% to 17% of the adult population in the United States and Europe.<sup>1,2</sup> Treatment options include medical and behavioral<sup>3</sup> therapy, intravesical injection<sup>4</sup> and surgery, such as bladder augmentation

or sacral neuromodulation.<sup>5</sup> Medical therapy with antimuscarinic agents decreases OAB symptom severity but some patients experience side effects, most commonly dry mouth.<sup>6</sup>

Although medication adherence is high in research trials, clinical stud-

### Abbreviations and Acronyms

ER = extended release

IR = immediate release

MPR = medication possession ratio

OAB = overactive bladder

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ies show that many patients discontinue medication.<sup>7</sup> Studies of pharmacy claims for antimuscarinic medications show that 37% to 68% of patients did not refill medication during the study period.<sup>8-10</sup> MPR represents the duration on medication compared to the total study period. The OAB medication MPR has been 0.34 to 0.45 in most studies except in a system with a \$5 to \$10 copayment per prescription, in which it was 0.64 to 0.83.<sup>8,11,12</sup> The medication adherence rate, that is the proportion of the study population with an MPR of greater than 0.8, has been 5% to 53%,<sup>8-11</sup> again with the highest rates in the system with low copayments. Medication adherence for ER formulations is higher than that for IR formulations.<sup>8,10</sup>

To our knowledge the reason for discontinuing this medication class has not been determined but it may be due to lack of efficacy, side effects or an unfavorable ratio of these factors. Another factor that may affect the risk-to-benefit ratio may be financial cost. American groups have examined medication adherence for antimuscarinic agents in settings in which patients pay at least a portion of the medication cost.<sup>8-12</sup> A study from the United Kingdom may have eliminated patient cost but was done before ER agents were available and before the current definitions of medication adherence were used in the literature.<sup>13</sup> Thus, we examined medication adherence in a setting in which ER formulations are provided free of charge to patients.

In the United States Military Health System medication dispensed at military treatment facilities is provided at no cost to patients. We hypothesized that this may alter the perceived cost-benefit ratio such that persistence and adherence may be different than previously noted in other American health care systems.

## MATERIALS AND METHODS

The study population consisted of military treatment facility enrollees in the National Capital Region who filled prescriptions for OAB medication during the study period. The National Capital Region encompasses treatment facilities in Virginia; Washington, D. C.; and Maryland. A computerized database was queried for all filled prescriptions for antimuscarinic agents from January 1, 2003 to December 31, 2005. The database contains demographic information on individuals eligible for military health care, and laboratory, radiology, pharmacy ordering and dispensing information.

Data on gender, dosing instructions, number of tablets dispensed, refill dates and whether the same individual had another medication of the same class prescribed during the study period were entered into a password protected and de-identified Excel® database. This study was approved under exempt status by the Walter Reed Army Medical Center and National Naval Medical Center institutional review boards.

The medication nonpersistence rate was defined as the proportion of patients who never refilled a prescription for any OAB medication during the 3-year study period. The medication switch rate was calculated as the proportion of patients who changed medication or dose at least once. This reporting is consistent with the previous literature.<sup>8-10</sup> The switch rate was calculated as a proportion of those who refilled at least once and as a proportion of the entire study sample. The Pearson chi-square test was used to determine statistical significance. MPR, defined as the total days of medication dispensed except for the last refill divided by the number of days between the first dispense date and the last refill date,<sup>10,11</sup> was calculated in patients who had at least 1 refill. Medication adherence, defined as in other studies as the proportion of patients with an MPR of 0.8 or greater, was calculated and compared using the Pearson chi-square test.<sup>8,10,12</sup>

During the study period oxybutynin IR, and tolterodine IR and ER were formulary medications but oxybutynin ER was not. For formulary medications no policy recommended 1 agent over another due to prescriber preference. Oxybutynin ER required a nonformulary medication request, a process that varies by pharmacy in the region, and ranged from a comment in the computerized ordering system to a form routed to the division head of the prescriber and then to the pharmacy for approval. It was recommended that another agent be tried before prescribing oxybutynin ER. The process of nonformulary medication request adds physician time but the medication is still at no cost to the patient.

MPRs were compared among groups using the Kruskal-Wallis test. Pairwise comparisons were made using the Mann-Whitney U test. The Bonferroni correction was applied when pairwise testing yielded statistically significant differences between groups. Medication persistence was examined using the Kaplan-Meier survival method. Patients were not considered to have failed to refill medication at the end of the study period unless they did not refill medication in the last 100 study days since most had 90-day refills. If they refilled within the last 100 study days, they were considered persistent from the first prescription through the 3-year mark. If they did not refill within the last 100 days, the last refill was considered the nonpersistence date. The log rank test was used to examine differences between survival curves. Statistical significance was considered at  $\alpha = 0.05$ . Data were analyzed using SPSS®, versions 13 and 16.

## RESULTS

Antimuscarinic medications were dispensed to 8,934 individuals in the 3-year study period. Of these patients 789 were prescribed clear instructions that medication was to be taken on an as needed basis for transient bladder spasms and not as chronic therapy. Thus, they were excluded from study, as were another 266 with pediatric dosing instructions and 21 adults with incomplete data available. The final study population consisted of 7,858 patients prescribed OAB medication, including 5,501 females (70%) and 2,357 males (30%).

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